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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,790	11/17/2000	Rupert Schmidt-Ullrich	02940139AA	3995

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WHITHAM, CURTIS & CHRISTOFFERSON, P.C.
11491 SUNSET HILLS ROAD
SUITE 340
RESTON, VA 20190

EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,790	SCHMIDT-ULLRICH ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-25 and 29-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-25 and 29-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20041229*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The amendments filed 12/29/04 render the restriction requirement moot, and have overcome the objections and the rejections under 35 USC §§ 112 and 102. Also, the declarations under 37 CFR 1.132 filed 12/29/04 are sufficient to overcome the rejection of claims 19-22, 30, 32 and 33 based upon Reardon et al.

Claim Rejections - 35 USC § 103

Claims 19-25 and 29-32 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Greene et al. (US 6,417,168) in view of Schmidt-Ullrich et al. (Proc. Amer. Assoc. Cancer Res. Annu. Meeting 39: 78, Abst. 533, March 1998); Wagner et al. (Int. J. Cancer 68(6): 782-787, 11 Dec. 1996); and Parker et al. (Proc. Amer. Assoc. Cancer Res. Annu. Meeting 38: 534, Abstr. 3581, April 1997) for the reasons of record set forth in the Office action of 9/9/04.

Applicant's arguments filed 12/29/04 have been fully considered but they are not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant presents arguments based upon evidence that was published after the effective filing date of the instant application that the choices of tyrosine kinase deficient ErbB family member binding protein exemplified or specifically described in Greene would be inferior to the C-terminally truncated, dominant

negative EGF-R (ErbB1) to which the claimed invention is limited. These arguments are not relevant to issue here, as the evidence presented does not show the state of the art at the time the invention was made. Applicant then goes on to characterize each of the secondary references as not anticipating the claimed invention (page 12). Applicant mischaracterizes the rejection here by arguing that Greene is taken in combination with Schmidt-Ullrich, and this combination is taken in combination with Wagner and Parker. Instead, the rejection is based upon combining Greene with Schmidt-Ullrich, Wagner and Parker together. The three secondary references together suggest at least three different reasons, or motivations, to use vectors encoding C-terminally truncated, dominant negative EGF-R in the method of Greene. Schmidt-Ullrich suggests that this recombinant protein would radiosensitize EGF-R expressing cancer cells transfected with the vector; Wagner suggests that this recombinant protein would sensitize EGF-R expressing cancer cells to the chemotherapeutic agent cisplatinum transfected with the vector; and Parker suggests that this recombinant protein would inhibit metastasis of EGF-R expressing cancer cells transfected with the vector. Applicant has not addressed the fact that rejection is based on the teachings provided by the combination of references.

Applicant does not dispute that the C-terminally truncated, dominant negative EGF-R of the claimed invention meets the requirement for a tyrosine kinase deficient ErbB family member binding protein that dimerizes with an ErbB family member in the generic invention disclosed by Greene, i.e. the instant invention is embraced by the generic invention of Greene. Nor does Applicant dispute that vectors encoding such proteins should be used to treat cancer in combination with either radiation or chemotherapy, or that such gene therapy would radiosensitize transfected cancer cells. Nor is it disputed that Greene does not disclose this

species of their generic invention. Nor is it disputed that each of Schmidt-Ullrich, Wagner, and Parker teach that transfection of specific cancer cells, each of which express EGF-R, with a vector expressing C-terminally truncated, dominant negative EGF-R negatively impacts those cancer cells *in vitro* and in the case of Parker, also *in vivo*, and each explicitly suggests such vectors *in vivo* may be useful to treat cancer related to expression of EGF-R.

Applicant points out that Greene presents no *in vivo* data (Reply, page 10), but does not develop any argument based upon this observation. Applicant points out that Schmidt-Ullrich does not discuss effective doses for *in* vivo use, and then makes unsupported assertions as to what one of skill in the art would or would not assume regarding enablement. First, Applicant is reminded that prior art references are presumed to be operable or enabling, and it is Applicant's burden to prove otherwise. MPEP 2121. Second, "[A]rgument of counsel cannot take the place of evidence lacking in the record." *In re Scarbrough*, 182 USPQ 298, 302 (CCPA 1974). Applicant is also reminded that positive results using model systems that are relevant to *in vivo* therapeutic use of a particular class of compound, e.g. the effect of a compound on cancer cells *in vitro*, are evidence that supports enablement of such therapeutic use, and that actual demonstration of clinical efficacy is not required to establish enablement. See *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995). Greene teaches in general that a vector expressing a tyrosine kinase deficient ErbB family member binding protein that dimerizes with an ErbB family member such as EGF-R, would be effective in treating cancer, and radiosensitize transfected cancer cells. Schmidt-Ullrich provides results obtained with a relevant model system suggesting that C-terminally truncated, dominant negative EGF-R has the properties taught by Greene.

Applicant also points out that Greene exemplifies different tyrosine kinase deficient proteins than C-terminally truncated, dominant negative EGF-R, and teaches that variants of p185 are preferred. The issue here is not whether Greene anticipates the instant claims, but whether Greene in combination with Schmidt-Ullrich, Wagner, and Parker would render the claimed invention obvious.

Applicant points out that Wagner and Parker do not teach that expression of C-terminally truncated, dominant negative EGF-R would radiosensitize the cancer cells, and argues there is no motivation to combine them with Greene and Schmidt-Ullrich. First, Greene had taught that expression of tyrosine kinase deficient ErbB family member binding protein would in general radiosensitize a transfected cancer cell. Schmidt-Ullrich presents experiments showing that C-terminally truncated, dominant negative EGF-R, in particular, also does so. What Parker and Wagner provide is additional motivation to use C-terminally truncated, dominant negative EGF-R in Greene's method. Second, recitation of "radiosensitizing cancer cells" in the preamble of claim 19 has little or no weight here. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where, as here, the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Greene discloses using the method for treating cancer with or without radiation,

and without radiation, Parker and Wagner both provide motivation to use C-terminally truncated, dominant negative EGF-R as the tyrosine kinase deficient ErbB family member binding protein in Greene's invention, regardless of whether radiation is also used.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER